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Health and Environmental Effects Profile for Decabromodiphenyl Oxide

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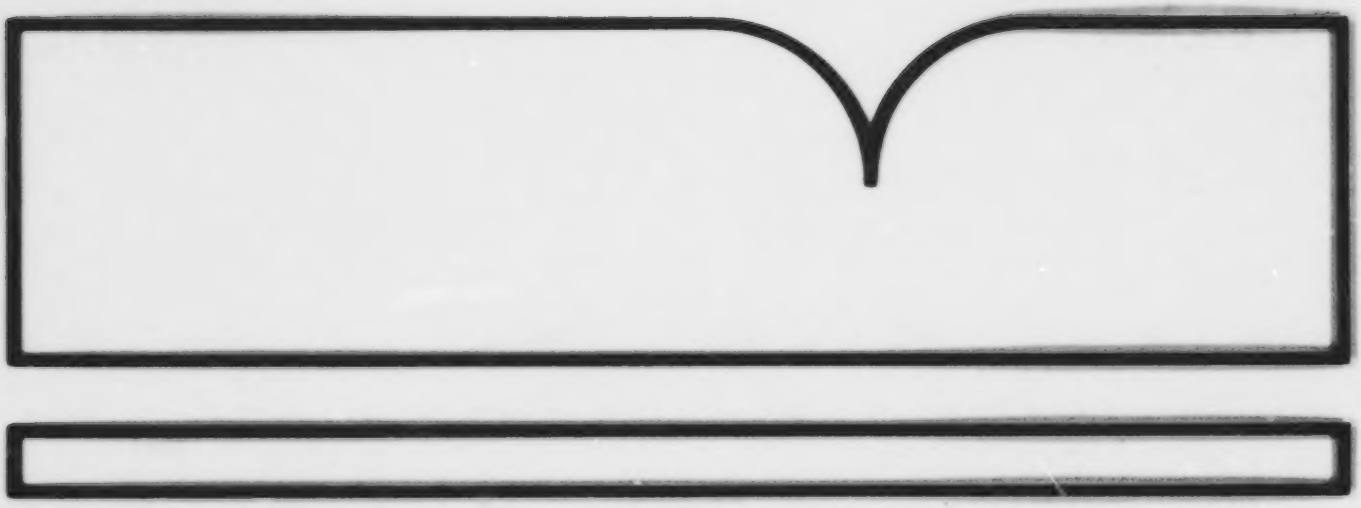

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16. ABSTRACT

The Health and Environmental Effects Profile for decabromodiphenyl oxide was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine a Reference Dose (RfD) or a carcinogenic potency factor for decabromodiphenyl oxide.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ value for decabromodiphenyl oxide is 1000.

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR DECABROMODIPHENYL OXIDE

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste and Emergency Response by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA), as well as to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched." The literature search material is current through November, 1985.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include Reference doses (RfDs) for chronic exposures. An RfD is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, RfDs are not estimated in this document series. Instead, a carcinogenic potency factor of q_1^* (U.S. EPA, 1980) is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

Reportable quantities (RQs) based on both chronic toxicity and carcinogenicity are derived. The RQ is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified under CERCLA. These two RQs (chronic toxicity and carcinogenicity) represent two of six scores developed (the remaining four reflect ignitability, reactivity, aquatic toxicity and acute mammalian toxicity).

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA and CERCLA dockets.

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EXECUTIVE SUMMARY

Decabromodiphenyl oxide is a common chemical name, but this compound is marketed industrially under the trade names FR-300-BA (Dow Chemical), Saytex 102 and 102E (Ethyl Corp.) and DE-83 and 83/R (Great Lakes Chemical). Various commercial products contain other brominated diphenyl oxides (such as nonabromodiphenyl oxide and octabromodiphenyl oxide) as impurities in amounts that may range from 22.6% (Norris et al., 1975) to <3% (CRCS, 1985). Decabromodiphenyl oxide dissolves slowly in organic solvents and is almost insoluble in water. Production in 1983 was estimated to be 19-25 million pounds (CRCS, 1985). Decabromodiphenyl oxide is used as a flame retardant additive for thermoplastics, thermoset resins and elastomeric polymers (Kuney, 1985).

Photodegradation should be a significant pathway for the environmental degradation of decabromodiphenyl oxide since it was experimentally found to photodegrade readily (Norris et al., 1973). Photodegradation may therefore occur in surface waters, atmospheres or on soil surfaces exposed to sunlight. Hydrolysis, oxidation and volatilization are not expected to be significant. Based on estimated K_{oc} values ranging from 16,900-300,000, decabromodiphenyl oxide may partition from the water column to sediments and is expected to be tightly bound to soil particles and, therefore, not leach in soils. Although decabromodiphenyl oxide did not bioconcentrate in rainbow trout during 48-hour static tests (Norris et al., 1973), the relatively high log K_{ow} value of 5.24 suggests a potential for bioaccumulation in aquatic ecosystems. The only biodegradation study specific to decabromodiphenyl oxide found it to be resistant to biodegradation using the Japanese MITI test (Sasaki, 1978). The inability of p-bromodiphenyl oxide to bio-

degrade, as determined by Tabak et al. (1981), may indicate that decabromodiphenyl oxide will also not biodegrade. Decabromodiphenyl oxide released to the atmosphere will most likely be associated with particulate matter that can be removed from air by wet and dry deposition. The significance of this physical removal mechanism in the determination of the overall residence time of this compound in the atmosphere is not known.

Decabromodiphenyl oxide may be emitted to the environment as a result of aqueous effluents and fugitive dust emissions from manufacture and use operations (CRCS, 1985). It has been detected in sludge, sediment and air particulate samples collected in the vicinity of manufacturing facilities (DeCarlo, 1979; Pellizzari et al., 1978). The compound has also been detected in composite hair samples obtained in Arkansas from barber shops near manufacturing facilities (DeCarlo, 1979). The incineration of plastics or other materials containing decabromodiphenyl oxide as a fire retardant may produce suspected highly toxic brominated dioxins in the atmosphere (Esposito et al., 1980).

Norris et al. (1973) found that rainbow trout did not accumulate decabromodiphenyl oxide to a measurable extent when exposed to 20 µg/ℓ for 48 hours.

Conclusions regarding the extent of gastrointestinal absorption of decabromodiphenyl oxide are not possible from the available data. Studies with ^{14}C-decabromodiphenyl oxide indicate that following oral dosing, rats excreted ~85-100% of the radioactivity in the feces and >1% in the urine within 24-72 hours (NTP, 1985; Norris et al., 1973, 1975; Kociba et al., 1975). While experiments in intact and bile duct-cannulated rats injected intravenously indicated that biliary excretion can be intensive (NTP, 1985), biliary excretion following oral dosing was not investigated.

Trace levels of radioactivity were detected in most tissues of rats 72 hours after dietary administration of ~250-50,000 ppm ^{14}C-decabromodiphenyl oxide for 1 day, with the highest systemic concentrations in the adipose tissue, liver and skin (NTP, 1985). ^{14}C was detected at trace levels only in adrenal and splenic tissue of rats 16 days after a single 1.0 mg/kg oral dose (Norris et al., 1973, 1975). Rats that were fed diets providing decabromodiphenyl oxide at doses of 0.1 or 1.0 mg/kg/day had significantly increased concentrations of bromine in the adipose tissue after 3 months (Kociba et al., 1975; Norris et al., 1973, 1975); the increases were dose-related and rose in a dose-related manner through 2 years of treatment. Bromine concentrations in the liver were slightly increased at 1.0 mg/kg/day after 12-24 months of exposure; increases in other tissues were not detected during the first 6 months of exposure or in any tissues at 0.01 mg/kg/day.

Fecal extracts from rats that were fed diets containing 250-50,000 ppm decabromodiphenyl oxide contained three main metbolites and unchanged parent compound (NTP, 1985). The metabolites were not identified and additional information characterizing metabolites of decabromodiphenyl oxide was not located.

Decabromodiphenyl oxide was tested for carcinogenicity in an NTP (1985) bioassay in which diets containing 0, 25,000 or 50,000 ppm of commercial grade compound (94-97% pure) were administered to groups of 50 male and 50 female F344-N rats and 50 male and 50 female B6C3F1 mice for 103 weeks. Daily dosages, estimated from food consumption data, were in the range of 1100-1200 and 2250-2500 mg/kg/day for the low- and high-dose rats and 3200-3800 and 6650-7800 mg/kg/day for the low- and high-dose mice. Some evidence of carcinogenicity was indicated by significantly increased

incidences of liver neoplastic nodules in the rats (low- and high-dose males, high-dose females). Equivocal evidence of carcinogenicity, as indicated by significantly increased incidences of hepatocellular adenomas or carcinomas (combined) and the presence of thyroid gland tumors, was found for male mice. Evidence of carcinogenicity was not observed in another dietary study in which groups of 25 male and 25 female Sprague-Dawley rats were administered much lower doses (0, 0.01, 0.1 or 1.0 mg/kg/day) of less pure (77.4%) compound for 2 years (Kociba et al., 1975; Norris et al., 1973, 1975).

Mutagenicity of decabromodiphenyl oxide was not demonstrated with or without metabolic activation in liquid suspension Ames assays with Salmonella typhimurium TA1535, TA1537, TA98 or TA100, in a mouse lymphoma L5178Y/TK$^{+/-}$ assay or in sister chromatid exchange or chromosomal aberrations assays in Chinese hamster ovary cells (NTP, 1985). Dietary administration of decabromodiphenyl oxide (77.4% pure) at doses of 0, 3, 30 or 100 mg/kg bw/day for 90 days before mating and during mating, gestation and lactation did not produce treatment-related increases in cytogenetic aberrations in bone marrow cells in maternal or neonatal Sprague-Dawley rats examined at weaning (Norris et al., 1975).

Teratogenicity or maternal toxicity was not observed in Sprague-Dawley rats administered 0, 10, 100 or 1000 mg/kg decabromodiphenyl oxide (77.4% pure) in corn oil by gavage on days 6-15 of gestation (Norris et al., 1973, 1975). Fetotoxicity was indicated by increased incidences of subcutaneous edema and delayed ossification of normally developed skull bones at 1000 mg/kg and resorptions at 10 and 100 mg/kg. Effects on reproductive capacity and neonatal development were not observed in Sprague-Dawley rats and offspring that were maintained on diets that provided 0, 3, 30 or 100 mg/kg/day

decabromodiphenyl oxide (77.4% pure) for 90 days before mating and during mating, gestation and lactation (Norris et al., 1975).

Treatment-related nonneoplastic lesions were observed in the NTP (1985) carcinogenesis bioassay in which F344-N rats and B6C3F1 mice of each sex were administered diets containing 0, 25,000 or 50,000 ppm decabromodiphenyl oxide (94-97%) for 103 weeks. Lesions included thrombosis and degeneration of the liver, fibrosis of the spleen, lymphoid hyperplasia of the mandibular lymph nodes and acanthosis of the forestomach in the high-dose male rats and hematopoiesis in the spleen in treated female rats. Nonneoplastic lesions in male mice included hypertrophy in the liver (low and high dose), granulomas in the liver (low dose) and follicular cell hyperplasia of the thyroid (low and high dose). An increased incidence of ulcers of the stomach occurred in the high-dose female mice. Dietary administration of 0, 3100, 6200, 12,500, 25,000 or 50,000 ppm decabromodiphenyl oxide for 13 weeks did not produce treatment-related effects (NTP, 1985).

No effects were observed in Sprague-Dawley rats that were administered diets providing decabromodiphenyl oxide (77.4% pure) dosages of 0, 0.01, 0.1 or 1.0 mg/kg/day for ~2 years (Kociba et al., 1975; Norris et al., 1973, 1975). Male Sprague-Dawley rats fed diets providing approximate doses of 0, 8, 80 or 800 mg/kg/day for 30 days had increased liver weights at 80 and 800 mg/kg/day, histological alterations in the liver (centrilobular cytoplasmic enlargement and vacuolation) and kidneys (hyaline degenerative cytoplasmic changes) at 800 mg/kg/day, and thyroid hyperplasia at 80 and 800 mg/kg/day (Norris et al., 1973, 1975).

Based on the NTP (1985) study showing 1) a dose-related increase in neoplastic nodules in male and female rats, 2) increased incidence of hepatocellular adenoma and carcinoma in male mice, the significance of which

was mitigated, however, by early mortality in control male mice, and 3) no other significant lesions in rats or mice, decabromodiphenyl oxide is classified in EPA Group C (U.S. EPA, 1986). An RQ of 1000 for chronic toxicity was derived based on the nonneoplastic liver and spleen effects in male rats in the NTP (1985) study.

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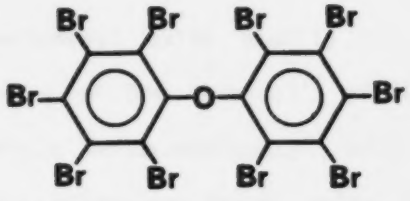
LIST OF ABBREVIATIONS

ABS	Acrylonitrile-butadiene-styrene
ADI	Acceptable daily intake
BCF	Bioconcentration factor
bw	Body weight
CAS	Chemical Abstract Service
CS	Composite score
EPDM	Ethylene-propylene rubber
GC/MS	Gas chromatography/mass spectrometry
HIPS	High impact polystyrene
K_{oc}	Soil sorption coefficient standardized with respect to soil organic matter
K_{ow}	Octanol/water partition coefficient
LDPE	Low density polyethylene
MED	Minimum effective dose
PBT	Polybutylene terephthalate
PCB	Polychlorinated biphenyl
ppb	Parts per billion
ppm	Parts per million
RQ	Reportable quantity
RV_d	Dose-rated value
RV_e	Effect-rated value
THF	Tetrahydrofuran
TWA	Time-weighted average
UV	Ultraviolet
WS	Water solubility

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Decabromodiphenyl oxide is also known as decabromodiphenyl ether, decabromophenyT ether, DBDPE, DBDPO, 1,1'-oxybis(2,3,4,5,6-pentabromobenzene), and bis(pentabromophenyl)ether and by the trade names FR-300-BA, Saytex 102, Saytex 102E, DE-83 and DE-83/R. The structure, molecular weight, empirical formula and CAS Registry number are as follows:



Molecular weight: 959.22

Empirical formula: $C_{12}Br_{10}O$

CAS Registry No.: 1163-19-5

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Commercial high purity grade decabromodiphenyl oxide is an off-white free-flowing powder (Ethyl Corp., 1986). Available physical properties are listed below:

Melting point:	295-305°C	Larson, 1979
Specific gravity:	3.04	Larson, 1979
Vapor pressure:		
at 250°C	<1 mm Hg	Norris et al., 1973
at 278°C	2 mm Hg	Norris et al., 1973
at 306°C	5 mm Hg	Norris et al., 1973
Water solubility:		
at 25°C	20-30 ppb	Norris et al., 1973

Solubility in organic solvents: (g/100 g solvent)		
acetone	0.05	Norris et al., 1973
benzene	0.48	Norris et al., 1973
chlorobenzene	0.60	Norris et al., 1973
methylene bromide	0.42	Norris et al., 1973
methylene chloride	0.09	Norris et al., 1973
o-xylene	0.87	Norris et al., 1973
Log K_{ow}:	5.24	Norris et al., 1973
	6.28 (estimated from water solubility data)	Lyman et al., 1982

Commercial decabromodiphenyl oxide usually contains other brominated diphenyl oxides. A sample of Dow Chemical's FR-300-BA decabromodiphenyl oxide was found to contain decabromodiphenyl oxide (77.4%), nonabromodiphenyl oxide (21.8%) and octabromodiphenyl oxide (0.8%) (Norris et al., 1975). The commercial product DE-83, produced by Great Lakes Chemical, reportedly is >97% decabromodiphenyl oxide and <3% other brominated diphenyl oxides (CRCS, 1985). Ethyl Corporation's Saytex 102E typically contains 97% decabromodiphenyl oxide (Ethyl Corp., 1986).

Decabromodiphenyl oxide is very stable thermally (decomposition temperature ~425°C), but is relatively unstable to UV radiation in compounds containing styrene structures (Larson, 1979).

1.3. PRODUCTION DATA

SRI (1985) listed as current manufacturers of decabromodiphenyl oxide the Ethyl Corp. (Magnolia, AR), Great Lakes Chemical Corp. (El Dorado, AR) and White Chemical Corp. (Newark, NJ). Ethyl Corp. markets the compound under the trade names Saytex 102 and Saytex 102E and Great Lakes Chemical markets it under the trade names DE-83/R and DE-83 (Kuney, 1985). Dow Chemical also produces decabromodiphenyl oxide under the trade name FR-300-BA, which reportedly produced 8-10 million pounds of this compound in 1982 (CRCS, 1985). Current production figures are not available; production in

1983 was estimated to be 19-25 million pounds (CRCS, 1985). Table 1-1 lists the public portion of the TSCA Inventory for 1977. The most recent import figure located for decabromodiphenyl oxide was 26.455 thousand pounds in 1982 (USITC, 1983).

Decabromodiphenyl oxide is manufactured by the bromination of diphenyl oxide in the presence of a Friedel-Crafts catalyst (Larson, 1979).

1.4. USE DATA

Decabromodiphenyl oxide is used as a flame retardant additive for thermoplastics, thermoset resins and elastomeric polymers such as nylon, polypropylene, LDPE, EPDM, HIPS, PBT, unsaturated polyesters and epoxies (Kuney, 1985). It is also widely employed as a flame retardant with antimony oxide in the high-impact polystyrene polymers used in the manufacture of television cabinets (Larson, 1979).

1.5. SUMMARY

Decabromodiphenyl oxide is a common chemical name, but this compound is marketed industrially under the trade names FR-300-BA (Dow Chemical), Saytex 102 and 102E (Ethyl Corp.) and DE-83 and 83/R (Great Lakes Chemical). Various commercial products contain other brominated diphenyl oxides (such as nonabromodiphenyl oxide and octabromodiphenyl oxide) as impurities in amounts that may range from 22.6% (Norris et al., 1975) to <3% (CRCS, 1985). Decabromodiphenyl oxide dissolves slowly in organic solvents and is almost insoluble in water. Production in 1983 was estimated to be 19-25 million pounds (CRCS, 1985). Decabromodiphenyl oxide is used as a flame retardant additive for thermoplastics, thermoset resins and elastomeric polymers (Kuney, 1985).

TABLE 1-1

Production Data for Decabromodiphenyl Oxide[a]

Manufacturer	Location	Production (pounds)
Dow Chemical	Midland, MI	1-10 million
Great Lakes Chemical	El Dorado, AR	confidential
Hexcel/Fine Organics[b]	Sayreville, NJ	1-10 million

[a]Source: U.S. EPA, 1983

[b]Hexcel/Fine Organics became Saytech, Inc., which has since been acquired by Ethyl Corp. (CRCS, 1985).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

2.1.1. Hydrolysis. Decabromodiphenyl oxide does not contain any functional groups that are likely to hydrolyze significantly under ambient conditions (Jaber et al., 1984); therefore, hydrolysis is not expected to be important.

2.1.2. Oxidation. Decabromodiphenyl oxide is expected to be inert to aquatic oxidation by RO_2 radical (Jaber et al., 1984). Based on a theoretically calculated rate constant for the atmospheric vapor-phase reaction of decabromodiphenyl oxide with HO radical (Section 2.2.), aquatic oxidation in sunlit natural water by HO radical is not expected to be significant in relation to photolysis.

2.1.3. Photolysis. Norris et al. (1973) studied the photolysis of decabromodiphenyl oxide in various solvents. Exposure of decabromodiphenyl oxide (7 ppm) in octanol, to a sunlamp of approximate sunlight intensity resulted in a photolytic half-life of 4 hours. A photodegradation half-life of 15 hours was measured in a xylene solvent with the formation of lower brominated diphenyl oxides. Norris et al. (1973) also exposed distilled water saturated with an excess of decabromodiphenyl oxide (1.25 g/ℓ) to sunlight for 98 days. A significant increase in bromine concentration in the water was found, relative to an unexposed 98-day sample. The concentration of bromine in the water in the exposed sample corresponded to ~300 times the initial amount of decabromodiphenyl oxide that was soluble in the water. In addition, the exposed sample showed significant discoloration compared with the unexposed sample. GC/MS analysis showed that the photodegradation products were not lower brominated diphenyl oxides. The authors

speculated that the decabromodiphenyl oxide degraded in water by a photohydroxylation process leading to the formation of phenolic compounds. The authors concluded that photodegradation should be a significant pathway for environmental degradation of decabromodiphenyl oxide.

2.1.4. **Microbial Degradation.** Decabromodiphenyl oxide was found to be degradation resistant using the Japanese MITI test (Sasaki, 1978); this biodegradation test involves use of an active sludge seed, 100 ppm test substance, and a 2-week incubation period. Other microbial studies specific to decabromodiphenyl oxide could not be located in the available literature.

Limited experimental data indicated that p-monobromodiphenyl oxide may be resistant to biodegradation in water even after microbial acclimation. Tabak et al. (1981) used a static-culture flask-screening procedure in which 5 and 10 ppm aqueous solution of p-bromodiphenyl oxide were incubated with a domestic wastewater microbial inoculum for 7 days followed by incubation in three weekly subcultures (totaling 28 days of incubation); p-bromodiphenyl oxide was not significantly degraded under the test conditions. Yagi and Sudo (1980) found that Alcaligenes BM-2, a strain of soil bacteria capable of using PCB (di-Cl) mixtures as the sole source of carbon, did not grow when p-bromodiphenyl oxide or p,p'-dibromodiphenyl oxide were used as sole carbon sources. These results suggest that decabromodiphenyl oxide will not significantly biodegrade in natural systems. Norris et al. (1973) speculated that decabromodiphenyl oxide is not readily metabolized by microorganisms.

2.1.5. **Volatilization.** Experimental water volatility data were not available. Estimation of Henry's Law constant based on the bond method of Hine and Mookerjee (1975) yields a value of ~2×10^{-10} atm-m³/mol. This value indicates that decabromodiphenyl oxide will not volatilize from water (Lyman et al., 1982).

2.1.6. Adsorption. Based on estimated K_{oc} values that range from 16,900-300,000 (Section 2.3.), partitioning of decabromodiphenyl oxide from the water column to particulate organic matter and sediment in water is potentially important.

2.1.7. Bioconcentration. Norris et al. (1973) exposed rainbow trout to 20 ppb ^{14}C-decabromodiphenyl oxide for 48 hours under static conditions. Analysis of filleted flesh from the exposed fish showed that decabromodiphenyl oxide did not bioconcentrate to a measurable extent. A PCB isomer (2,2',4,4'-tetrachlorobiphenyl) with known bioconcentration properties was used as a positive control; it bioconcentrated ~50 times over initial exposure levels within 4 hours.

Although decabromodiphenyl oxide did not bioconcentrate in the above rainbow trout test, the relatively high log K_{ow} value (5.24) for decabromodiphenyl oxide (Norris et al., 1973) suggests a potential for bioaccumulation in aquatic ecosystems. Estimation of BCF can be made by use of the following recommended equations (Lyman et al., 1982):

$$\text{Log BCF} = 0.76 \text{ Log } K_{ow} - 0.23 \qquad (2\text{-}1)$$

$$\text{Log BCF} = 2.791\text{-}0.564 \text{ Log WS (in ppm)} \qquad (2\text{-}2)$$

Based on a log K_{ow} of 5.24 and a WS of 20-30 ppb at 25°C (Norris et al., 1973), the BCF values calculated from Equations 2-1 and 2-2 are 5650 and 4950, respectively. These BCF values suggest that decabromodiphenyl oxide may significantly bioconcentrate in aquatic organisms.

2.2. AIR

Decabromodiphenyl oxide is not expected to volatilize from water (see Section 2.1.5.). In addition, its relatively low vapor pressure (<1 mm Hg at 250°C) suggests that volatilization to the atmosphere at ambient temperatures will not be significant. Decabromodiphenyl oxide released to the

atmosphere will most likely be associated with particulate matter. Decabromodiphenyl oxide air particulates have been monitored in the vicinity of manufacturing facilities (DeCarlo, 1979). Atmospheric particulates can be physically removed from air by wet and dry deposition.

Decabromodiphenyl oxide is susceptible to significant photodegradation (see Section 2.1.3.). Chemical transformation by direct photolysis in sunlit atmospheres is therefore possible.

The rate constant for the vapor-phase reaction of decabromodiphenyl oxide with photochemically produced HO radical has been theoretically calculated to be 8.262×10^{-14} cm³/molecule-sec at 25°C (U.S. EPA, 1985). Assuming an atmospheric concentration of 8×10^5 HO radical/cm³, the calculated half-life for this reaction is 4.05 months (U.S. EPA, 1985).

2.3. SOIL

Experimental data pertaining to the fate of decabromodiphenyl oxide in soil could not be located in the available literature. Available microbial degradation data (see Section 2.1.4.) indicate that decabromodiphenyl oxide is resistant to biodegradation. Because decabromodiphenyl oxide is susceptible to photodegradation in the solution phase (see Section 2.1.3.), it may undergo photolysis from soil surfaces when exposed to sunlight.

Table 2-1 lists various equations that may be used to estimate K_{oc} from WS and log K_{ow} values. The estimated K_{oc} values range from 16,900-300,000, which indicates that decabromodiphenyl oxide will be tightly bound in soil and is not expected to leach.

2.4. SUMMARY

Photodegradation should be a significant pathway for the environmental degradation of decabromodiphenyl oxide since it was experimentally found to photodegrade readily (Norris et al., 1973). Photodegradation may therefore

TABLE 2-1

Estimation of K_{oc} for Decabromodiphenyl Oxide

Equation[a,b]	Estimated K_{oc} Value
Log K_{oc} = 3.64-0.55 log WS (in ppm)	33,200
Log K_{oc} = 0.44-0.54 log WS (in mol fraction)	300,000
Log K_{oc} = 0.544 log K_{ow} + 1.377	16,900
Log K_{oc} = 0.937 log K_{ow} - 0.006	80,000
Log K_{oc} = 1.00 log K_{ow} - 0.21	107,000

[a]Source: Lyman et al., 1982

[b]Log K_{ow} = 5.24 and WS = 20-30 ppb (Norris et al., 1973)

occur in surface waters, atmospheres or on soil surfaces exposed to sunlight. Hydrolysis, oxidation and volatilization are not expected to be significant. Based on estimated K_{oc} values ranging from 16,900-300,000, decabromodiphenyl oxide may partition from the water column to sediments and is expected to be tightly bound to soil particles and, therefore, not leach in soils. Although decabromodiphenyl oxide did not bioconcentrate in rainbow trout during 48-hour static tests (Norris et al., 1973), the relatively high log K_{ow} value of 5.24 suggests a potential for bioaccumulation in aquatic ecosystems. The only biodegradation study specific to decabromodiphenyl oxide found it to be resistant to biodegradation using the Japanese MITI test (Sasaki, 1978). The inability of p-bromodiphenyl oxide to biodegrade, as determined by Tabak et al. (1981), may indicate that decabromodiphenyl oxide will also not biodegrade. Decabromodiphenyl oxide released to the atmosphere will most likely be associated with particulate matter that can be removed from air by wet and dry deposition. The significance of this physical removal mechanism in the determination of the overall residence time of this compound in the atmosphere is not known.

3. EXPOSURE

3.1. WATER

Decabromodiphenyl oxide was qualitatively identified by GC/MS in sludge samples obtained from a polybrominated biphenyl manufacturing facility discharge zone in Bayonne, NJ (DeCarlo, 1979). Sediment samples collected in the vicinity of the Great Lakes Chemical Corp., which manufactures brominated organics in El Dorado, AR, were found to contain maximum decabromodiphenyl oxide concentrations of 1000 mg/kg (Pellizzari et al., 1978). The U.S. EPA STORET Data Base contained no observations for decabromodiphenyl oxide.

Exposure of decabromodiphenyl oxide to the water environment may result from aqueous effluents from manufacturing and user industries (CRCS, 1985). Norris et al. (1973) tested the aqueous leachability of decabromodiphenyl oxide from polystyrene and ABS polymer systems containing the compound as a flame retardant; migration of decabromodiphenyl oxide within the polymer system was not significant and extraction of decabromodiphenyl oxide was primarily due to the erosion of surface particles. This may suggest that leaching of decabromodiphenyl oxide from plastics disposed of in landfills may not be significant. In addition, decabromodiphenyl oxide that may be leached from landfill materials is likely to become tightly adsorbed to soil particles (see Section 2.3.) and, therefore, may not leach significantly to groundwaters.

3.2. FOOD

Data pertaining to the monitoring of decabromodiphenyl oxide in foods could not be located in the available literature as cited in the Appendix.

3.3. INHALATION

DeCarlo (1979) reported the detection of decabromodiphenyl oxide in air particulates in Arkansas in the vicinity of brominated organic manufacturing facilities. Ambient air samples collected at the Great Lakes Chemical manufacturing facility (El Dorado, AR) contained maximum levels of 98,118 ng/m³, while samples collected at the Velsicol facility (El Dorado, AR) contained a maximum level of 72 ng/m³ (Pellizzari et al., 1978).

Decabromodiphenyl oxide may enter the air environment as fugitive dust emissions from manufacturing and user facilities (CRCS, 1985).

Industrial hygiene surveys have determined employee 8-hour TWA exposures to decabromodiphenyl oxide of 1-4 mg/m³ with short-term levels as high as 42 mg/m³ (AIHA, 1981). During a dumping operation performed by workers wearing respirators, the maximum airborne level of 400 mg/m³ was measured for decabromodiphenyl oxide (AIHA, 1981).

The incineration of plastics on other materials containing decabromodiphenyl oxide as a fire retardant may produce suspected highly toxic brominated dioxins in the atmosphere (Esposito et al., 1980), although brominated dioxins have never been reported in atmospheric samples.

3.4. DERMAL

DeCarlo (1979) reported the detection of decabromodiphenyl oxide in human hair samples obtained at large from El Dorado and Magnolia, AR. Of three composite hair samples analyzed, one contained levels of 5 µg/kg while another contained lower levels. The survey included a total of ~40 individuals, indicating that a minimum of 5% (2/40) of the population had detectable levels of decabromodiphenyl oxide.

3.5. SUMMARY

Decabromodiphenyl oxide may be emitted to the environment as a result of aqueous effluents and fugitive dust emissions from manufacture and use operations (CRCS, 1985). It has been detected in sludge, sediment and air particulate samples collected in the vicinity of manufacturing facilities (DeCarlo, 1979; Pellizzari et al., 1978). The compound has also been detected in composite hair samples obtained in Arkansas from barber shops near manufacturing facilities (DeCarlo, 1979). The incineration of plastics or other materials containing decabromodiphenyl oxide as a fire retardant may produce suspected highly toxic brominated dioxins in the atmosphere (Esposito et al., 1980).

4. PHARMACOKINETICS

4.1. ABSORPTION

The disposition of decabromodiphenyl oxide (97.9-99.2% pure) was investigated in groups of three male F344-N rats as part of a carcinogenesis bioassay that was available as a board draft (NTP, 1985). In these experiments, the compound was administered to male F344/N rats in the diet at concentrations of ~250-50,000 ppm for 9, 10 or 11 days. On day 8, the test diet contained ^{14}C-decabromodiphenyl oxide, while unlabeled compound was administered on the other days. Urine and feces were collected for up to 72 hours after the labeled compound was given and analyzed for radioactivity. At the end of the study period, the rats were killed and samples of blood, liver, kidney, lung, muscle, fat, skin (ear), brain, gut contents and gut tissue were analyzed for radioactivity. Regardless of dosing schedule, the feces collected over 72 hours contained 82-100% of the dose of radioactivity. All tissues contained measurable levels ($\geq$0.001-0.449% of the dose) of radioactivity except the brain. Urine collected over 72 hours contained $\leq$0.012% of the dose. In another experiment, rats were injected intravenously with 1.07 mg/kg ^{14}C-decabromodiphenyl oxide. At 72 hours after injection, the feces and gut contents contained 74% of the dose, indicating a high degree of biliary excretion. The percentages of urinary and tissue radioactivity were ~10-100 times higher at 72 hours following intravenous dosing than at 72 hours following oral dosing. NTP (1985) attempted to calculate the extent of gastrointestinal absorption by comparing the tissue and urine levels and concluded that gastrointestinal absorption was minimal.

4.2. DISTRIBUTION

Analysis of the major organs and tissues in the NTP (1985) studies of diet-administered ^{14}C-decabromodiphenyl oxide (see Section 4.1.) showed

trace levels of radioactivity in most tissues, with the highest concentrations in the gastrointestinal tissue, skin, adipose tissue and liver.

Norris et al. (1973, 1975) administered a single 1.0 mg/kg dose of ^{14}C-labeled decabromodiphenyl oxide in corn oil to male and female Sprague-Dawley rats. Tissues from three rats/sex were examined for radioactivity on days 1, 3 and 16. After 16 days, ^{14}C was detected only in adrenal and splenic tissue (0.01%±0.06 and 0.06%±0.07 of the dose administered/g of tissue, respectively); radioactivity was not detected in adipose, heart, skin, liver or pancreas tissue. It was detected in all tissues examined on day 1, but actual test results from days 1 and 3 were not reported.

Tissue bromine content was determined in Sprague-Dawley rats that were fed diets that provided decabromodiphenyl oxide (77.4%) at dosages of 0, 0.01, 0.1 or 1.0 mg/kg/day (Kociba et al., 1975; Norris et al., 1973, 1975). Analyses were performed on groups of 2-6 rats containing both sexes after 0, 0.33, 1, 3, 6, 12, 18 and 23-24 months of exposure. Bromine concentrations in kidney, skeletal muscle, serum and testis tissue samples did not increase during the first 6 months of the study at any of the dose levels and these tissues were not analyzed subsequently. Bromine concentrations in the liver were slightly increased at the high dose after 12-24 months of exposure, suggesting that a low-level steady-state condition had been reached. Adipose tissue bromine concentrations were significantly increased at the 0.1 and 1.0 mg/kg/day levels after 3 months of treatment. The increases were related to dose and continued to rise in a dose-related manner during the second year of treatment.

4.3. METABOLISM

Benzene and tetrahydrofuran extracts of feces that were collected from groups of three male F344 rats fed diets containing ~250, 500, 2500, 5000, 25,000 or 50,000 ppm decabromodiphenyl oxide were analyzed by high-performance liquid chromatography (NTP, 1985). Unchanged decabromodiphenyl oxide and three main (unidentified) metabolites were reported. Unmetabolized decabromodiphenyl oxide accounted for most of the excreted material, as total recovery was in the range of 86.5-98.4% in the four lowest dose groups; recovery was 72.1 and 78.5% at 25,000 and 50,000 ppm, respectively, but these data were considered equivocal because of low recovery resulting from analytical problems.

Data on the metabolites of decabromodiphenyl oxide could not be located in the available literature.

4.4. EXCRETION

Decabromodiphenyl oxide was administered to groups of male F344-N rats in the diet at concentrations of ~250-50,000 ppm for up to 11 days (NTP, 1985) (see Section 4.1.). On day 8, the diets contained ^{14}C-decabromodiphenyl oxide (NTP, 1985). Examination of the feces showed that ~82-100% of the administered radioactivity was recovered in the feces within 72 hours. Recovery was not related to dose, and most of the radioactivity was eliminated in the first 24 hours. Urinary excretion accounted for ~0.01% of the ingested radioactivity. Results of experiments in intact and bile duct-cannulated rats dosed intravenously with ^{14}C-decabromodiphenyl oxide indicate that much of the fecal excretion may be accounted for by biliary excretion; however, NTP (1985) did not study biliary excretion in orally dosed rats (see Section 4.1.).

^{14}C-Decabromodiphenyl oxide (77.4% pure) in corn oil was given orally (presumably intubation) to three male and three female Sprague-Dawley rats at a dose of 1.0 mg/kg (Norris et al., 1973, 1975); 90.6 and >99% of the administered radioactivity was detected in the feces after 24 and 48 hours, respectively. Less than 1% of the radioactivity was eliminated in the urine and expired air when measured at 24-hour intervals for 16 days.

4.5. SUMMARY

Conclusions regarding the extent of gastrointestinal absorption of decabromodiphenyl oxide are not possible from the available data. Studies with ^{14}C-decabromodiphenyl oxide indicate that following oral dosing, rats excreted ~85-100% of the radioactivity in the feces and >1% in the urine within 24-72 hours (NTP, 1985; Norris et al., 1973, 1975; Kociba et al., 1975). While experiments in intact and bile duct-cannulated rats injected intravenously indicated that biliary excretion can be intensive (NTP, 1985), biliary excretion following oral dosing was not investigated.

Trace levels of radioactivity were detected in most tissues of rats 72 hours after dietary administration of ~250-50,000 ppm ^{14}C-decabromodiphenyl oxide for 1 day, with the highest systemic concentrations in the adipose tissue, liver and skin (NTP, 1985). ^{14}C was detected at trace levels only in adrenal and splenic tissue of rats 16 days after a single 1.0 mg/kg oral dose (Norris et al., 1973, 1975). Rats that were fed diets providing decabromodiphenyl oxide at doses of 0.1 or 1.0 mg/kg/day had significantly increased concentrations of bromine in the adipose tissue after 3 months (Kociba et al., 1975; Norris et al., 1973, 1975); the increases were dose-related and rose in a dose-related manner through 2 years of treatment.

Bromine concentrations in the liver were slightly increased at 1.0 mg/kg/day after 12-24 months of exposure; increases in other tissues were not detected during the first 6 months of exposure or in any tissues at 0.01 mg/kg/day.

Fecal extracts from rats that were fed diets containing 250-50,000 ppm decabromodiphenyl oxide contained three main metabolites and unchanged parent compound (NTP, 1985). The metabolites were not identified and additional information characterizing metabolites of decabromodiphenyl oxide was not located.

5. EFFECTS

5.1. CARCINOGENICITY

A NTP (1985) carcinogenesis bioassay of decabromodiphenyl oxide was available as a board draft. Diets containing 0, 25,000 or 50,000 ppm of commercial grade compound (94-97% pure) were fed to groups of 50 male and 50 female F344-N rats and 50 male and 50 female B6C3F1 mice for 103 weeks. Average daily dosages were estimated from food consumption data to be 1119 and 2236 mg/kg for the low- and high-dose male rats, 1199 and 2553 mg/kg for the low- and high-dose female rats, 3203 and 6645 mg/kg for the low- and high-dose male mice, and 3758 and 7776 mg/kg for the low- and high-dose female mice. The rats and mice were maintained without treatment for an additional 1 and 0-1 weeks, respectively, and then sacrificed. All animals were observed daily and body weights were measured weekly for the first 12 weeks of the study and monthly thereafter. Comprehensive gross and histological examinations were performed on all animals, including those that were moribund or that died during the study (unless precluded by autolysis or cannibalization).

Significant treatment-related effects on food consumption, body weight or clinical signs of toxicity were not reported for any rats (NTP, 1985). Although survival of the low-dose male rats was significantly lower than that of the controls after week 102, the decrease was observed late in the study and no reduced survival occurred in any other group; therefore, NTP (1985) concluded that the decreased survival in the low-dose male rats may not have been compound-related. As detailed in Table 5-1, neoplastic nodules occurred in the livers of male and female rats at incidences that were dose-related and statistically significant. The incidence of hepatocellular carcinoma alone was 1/50 control males, 1/50 low-dose males, 1/49

TABLE 5-1

Carcinogenicity of Technical Grade Decabromodiphenyl Oxide in F344/N Rats and B6C3F1 Mice Exposed in Diet[a]

Species	Sex	Exposure (dose)[b]	Duration of Treatment (weeks)	Duration of Study (weeks)	Target Organ	Tumor Type	Tumor Incidence (p_1 value)[c]
Rat	M	0 ppm	103	104	liver	neoplastic nodule	1/50 (p<0.001)
						neoplastic nodule or hepatocellular carcinoma	2/50 (p<0.001)
		25,000 ppm (1119 mg/kg/day)	103	104	liver	neoplastic nodule	7/50 (p=0.030)
						neoplastic nodule or hepatocellular carcinoma	8/50 (p<0.046)
		50,000 ppm (2236 mg/kg/day)	103	104	liver	neoplastic nodule	15/49 (p<0.001)
						neoplastic nodule or hepatocellular carcinoma	15/49 (p<0.001)
	F	0 ppm	103	104	liver	neoplastic nodule	1/50 (p=0.004)
						neoplastic nodule or hepatocellular carcinoma	1/50 (p=0.006)
		25,000 ppm (1119 mg/kg/day)	103	104	liver	neoplastic nodule	3/49 (p=0.301)
						neoplastic nodule or hepatocellular carcinoma	5/49 (p=0.098)
		50,000 ppm (2553 mg/kg/day)	103	104	liver	neoplastic nodule	9/50 (p=0.008)
						neoplastic nodule or hepatocellular carcinoma	9/50 (p=0.008)
Mouse	M	0 ppm	103	103-104	liver	hepatocellular adenoma	4/50 (p=0.027)
						hepatocellular carcinoma	5/50 (p=0.258)
						hepatocellular adenoma or carcinoma	8/50 (p=0.021)
					thyroid	follicular cell adenoma	0/50 (p=0.101)
						follicular cell adenoma or carcinoma	0/50 (p=0.118)
	M	25,000 ppm (3203 mg/kg/day)	103	103-104	liver	hepatocellular adenoma	12/50 (p=0.027)
						hepatocellular carcinoma	14/50 (p=0.020)
						hepatocellular adenoma or carcinoma	22/50 (p=0.002)
					thyroid	follicular cell adenoma	3/50 (p=0.121)
						follicular cell adenoma or carcinoma	4/50 (p=0.059)
Mouse	M	50,000 ppm (6645 mg/kg/day)	103	103-104	liver	hepatocellular adenoma	12/50 (p=0.027)
						hepatocellular carcinoma	8/50 (p=0.277)
						hepatocellular adenoma or carcinoma	18/50 (p=0.019)
					thyroid	follicular cell adenoma	3/50 (p=0.121)
						follicular cell adenoma or carcinoma	3/50 (p=0.121)

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QUALITY OF EVIDENCE

Strengths of Study:	The compound was administered by a relevant route at two dose levels to both sexes of two species. A large number of animals in each group were treated for the lifespan. Comprehensive histological examinations and appropriate statistical analyses were performed.
Weakness of Study:	High mortality of control male mice early in the study, presumably from fighting, may have weakened the evidence of carcinogenicity in male mice.
Overall Adequacy:	Adequate
Comments:	Compound 94-97% pure. No evidence of carcinogenicity in female B6C3F1 mice similarly exposed to 25,000 ppm (3758 mg/kg/day) or 50,000 ppm (7776 mg/kg/day).

[a]Source: NTP, 1985

[b]Average daily dosages, estimated by NTP (1985) from food consumption data

[c]P values from the Cochran-Armitage trend test and Fisher Exact test indicated with the incidences for the control group and dosed groups, respectively.

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high-dose males, 0/50 control females, 2/49 low-dose females and 0/50 high-dose females and not related to treatment. The increased incidences of neoplastic nodules were considered as some evidence of decabromodiphenyl oxide carcinogenicity in male and female rats by NTP (1985).

Treatment-related effects on body weight or clinical signs of toxicity or survival were not observed in any of the groups of mice of either sex (NTP, 1985). Losses of control male mice were significant during the first year of the study, but were comparable to the dosed mice after that point; the early losses were presumed to be due to fighting. Statistically significant increased incidences of hepatocellular adenomas or carcinomas (combined) occurred in the male mice (see Table 5-1). The incidence of hepatocellular carcinoma alone, however, was not significantly increased in the high-dose mice. Thyroid gland follicular cell adenomas or carcinomas (combined) also occurred in the treated male mice, but the increases were not statistically significant. Increased incidences of neoplastic lesions were not observed in the female mice. The evidence of carcinogenicity in the male mice was considered to be limited by the early loss of the control animals. NTP (1985) concluded that the significantly increased incidence of hepatocellular adenomas and carcinomas (combined) in the low-dose male mice and the increased incidence of thyroid gland tumors in both male groups represented equivocal evidence of carcinogenicity in male mice. There was no evidence of carcinogenicity in female mice.

Groups of 25 male and 25 female Sprague-Dawley (Spartan substrain) rats were administered decabromodiphenyl oxide in the diet at dosages of 0, 0.01, 0.1 or 1.0 mg/kg bw/day in a 2-year study (Kociba et al., 1975; Norris et al., 1973, 1975). The sample used in this study contained 77.4% decabromodiphenyl oxide, 21.8% nonabromodiphenyl oxide and 0.8% octabromodiphenyl oxide.

Necropsies that included comprehensive histological examinations were conducted on all rats that died during the study and those sacrificed at termination (day 702 for the males and day 735 for the females). Treatment-related neoplastic effects, as indicated by number of rats that developed tumors, total number of tumors, specific types of tumors or combined male and female data, were not observed at any dose level. Treatment-related effects on body weight, survival and other indices of toxicity (Section 5.5.) were not observed.

5.2. MUTAGENICITY

Mutagenicity studies of decabromodiphenyl oxide were conducted in conjunction with the NTP (1985) carcinogenicity bioassay, apparently because mutagenicity data are unavailable in the published literature. Presumably the commercial grade compound used in the carcinogenicity study was assayed.

Decabromodiphenyl oxide was not mutagenic in Salmonella typhimurium strains TA1535, TA1537, TA98 or TA100 when tested in a liquid suspension assay with or without Aroclor 1254-induced male Sprague-Dawley rat or male Syrian hamster S-9 preparations (NTP, 1985). Doses ranged from 100-10,000 µg/plate.

Decabromodiphenyl oxide was not mutagenic in the mouse lymphoma L5178Y/TK$^{+/-}$ assay when tested with or without Aroclor 1254-induced male F344 rat liver S-9 preparation at doses of 7-10 µg/mℓ (NTP, 1985).

Sister chromatid exchanges or chromosomal aberrations were not induced in Chinese hamster ovary cells treated in vitro with decabromodiphenyl oxide at doses of 50-500 µg/mℓ with or without Aroclor 1254-induced male Sprague-Dawley rat liver S-9 preparation (NTP, 1985).

Norris et al. (1975) administered diets that provided 0, 3, 30 or 100 mg decabromodiphenyl oxide/kg bw/day to male and female Sprague-Dawley rats

(numbers not specified) for 90 days before and during mating, gestation and lactation. Compound purity was 77.45% (see Section 5.1.). Cytogenetic examination of bone marrow cells from the parental animals and neonates at weaning (day 21) showed no treatment-related increase in cytogenetic aberrations.

5.3. TERATOGENICITY

Decabromodiphenyl oxide (77.4%) was administered by gavage in corn oil suspension at doses of 0, 10, 100 or 1000 mg/kg/day to an unspecified number of Sprague-Dawley rats on days 6-15 of gestation (Norris et al., 1973, 1975). There was no evidence of teratogenicity at any of the dose levels, but there was an increased number of litters with subcutaneous edema and delayed ossification of normally developed skull bones at 1000 mg/kg. Fetotoxicity was also indicated by a significantly increased incidence of resorptions, but this effect occurred only at 10 and 100 mg/kg and not in the high-dose group. Other fetotoxicity indices were unremarkable (position and number of fetuses in utero, number of corpora lutea, fetal weight, crown/rump ratio and male/female sex ratio). Maternal toxicity was not indicated by effects on appearance and demeanor, food consumption, body and liver weights. Analysis of maternal and fetal livers for bromine revealed statistically significant increased concentrations only in the maternal rats receiving 1000 mg/kg/day; concentrations were not increased in any of the fetal groups.

5.4. OTHER REPRODUCTIVE EFFECTS

Norris et al. (1975) administered diets that provided decabromodiphenyl oxide (77.4%) at doses of 0, 3, 30 or 100 mg/kg bw/day to an unspecified number of female Sprague-Dawley rats for 90 days before and during mating, gestation and lactation. Treatment-related effects on reproductive capacity

and neonatal development were not indicated by evaluation of length of time between the first day of cohabitation and parturition, number of live and dead newborn, number of live pups at days 1, 7, 14 and 21, litter weights at days 1, 7 and 14, individual weaning weights at day 21, weanling sex ratios on days 1 and 21, and necropsies of the weanlings (including organ weight determination and unspecified gross and histological examinations) on day 21. Maternal effects were not indicated by body weight and food consumption measurements during the study and necropsies at weaning. Additional information regarding this study, such as the number of neonates and litters examined, was not reported.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Groups of 50 F344-N rats and 50 B6C3F1 mice of each sex were administered diets containing 0, 25,000 or 50,000 ppm of commercial grade (94-97% pure) decabromodiphenyl oxide for 103 weeks in an NTP (1985) carcinogenesis bioassay (see Section 5.1.). Increased incidences of nonneoplastic lesions were observed in several tissues of the dosed rats and mice, and included thrombosis (control, 1/50; low-dose, 0/50; high-dose, 9/49) and degeneration (13/50; 19/50; 22/50) in the liver, fibrosis of the spleen (5/49; 8/50; 13/49), lymphoid hyperplasia of the mandibular lymph nodes (4/50; 6/50; 13/49) and acanthosis of the forestomach (0/49; 2/50; 5/49) in the high-dose male rats. The incidence of hematopoiesis in the spleen (12/49; 24/48; 17/50) was slightly increased in the female rats. Degeneration of the eye occurred at an increased incidence in the low-dose female rats (5/50; 15/50; 1/50), but this reportedly could have resulted from greater exposure to fluorescent light. In the male mice, centrilobular hypertrophy (0/50; 34/50; 32/50) and granulomas (8/50; 22/50; 12/50) of the liver occurred at increased incidences. Follicular cell hyperplasia of the thyroid was

increased in the male mice (4/50; 10/50; 19/50). An increased incidence of ulcers of the stomach (1/50; 1/50; 8/50) occurred in the high-dose female mice.

Groups of 10 F344-N rats and 10 B6C3F1 mice of each sex were administered diets containing 0, 3100, 6200, 12,500, 25,000 or 50,000 ppm decabromodiphenyl oxide for 13 weeks in range-finding studies for the NTP (1985) bioassay. Treatment-related effects on body weight, feed consumption, clinical signs, survival and tissues, as indicated by comprehensive gross and microscopic examination, were not observed.

Decabromodiphenyl oxide was administered to groups of 25 male and 25 female Sprague-Dawley rats in the diet at dosages of 0, 0.01, 0.1 or 1.0 mg/kg bw/day for ~2 years (Kociba et al., 1975; Norris et al., 1973, 1975). The decabromodiphenyl oxide used in this study was only 77.4% pure (21.8% nonabromodiphenyl oxide and 0.8% octabromodiphenyl oxide). Observations for changes in appearance and demeanor were conducted daily, body weights were determined weekly for the first 6 months and biweekly thereafter, and food consumption was determined weekly for the first 3 months and during 1 week of each succeeding month. Blood and urine samples were collected from three to five rats/sex (five rats/sex sampled when not precluded by mortality) at ~1 year (361 days) and 2 years (695 days for males and 723 days for females) for hematological analysis and urinalysis. Blood serum samples were collected from all rats necropsied at the end of the study (3-7 males on day 702, 9-10 females on day 735) for clinical chemistry determinations. Comprehensive gross and histological examinations were conducted on all rats at the end of the study; pathological examinations were also conducted on all rats that died during the course of the study, but histological examinations of these animals were limited to tissues with gross lesions or tissues

needed to ascertain probable cause of death. Gross and limited pathological tests were also performed on five rats/sex/dose sacrificed after 3 months in a related experiment involving collection of tissues for bromine analysis. Treatment-related toxicological effects, as indicated by the above endpoints (including organ weights) were not discerned. The related experiment indicated tissue accumulation of bromine in similarly-exposed rats.

Groups of five male Sprague-Dawley rats were fed diets containing 0, 0.01, 0.1 or 1.0% decabromodiphenyl oxide (approximate doses of 0, 8, 80 or 800 mg/kg bw/day, respectively) for 30 days (Norris et al., 1973, 1975). No treatment-related effects on appearance, demeanor, food consumption or body weight during the study or hematological or urinalysis indices during the terminal week of the study were observed. Gross and histological examinations were conducted at the end of the study; effects included increased liver weights at 80 and 800 mg/kg/day and histological alterations in the liver (centrilobular cytoplasmic enlargement and vacuolation) and kidneys (hyaline degenerative cytoplasmic changes) at 800 mg/kg/day. Dose-related thyroid hyperplasia occurred in rats at both 80 and 800 mg/kg/day. The incidences of the above lesions and the extent of histological examinations were not indicated; however, effects were not observed at 8 mg/kg/day.

5.6. OTHER RELEVANT INFORMATION

Groups of five F344-N rats and five B6C3F1 mice of each sex were administered decabromodiphenyl oxide in the diet at 0-100,000 ppm for 14 days (NTP, 1985). There were no deaths, clinical signs or gross pathological lesions and no effects on body weights in any group.

Administration of single doses of decabromodiphenyl oxide by gavage at levels of 126, 252, 500, 1000 or 2000 mg/kg (10% corn oil suspensions) did not produce signs of toxicity or gross pathological changes in female Sprague-Dawley rats during a 14-day observation period (Norris et al., 1973, 1975). The number of rats tested per dose were not specified, but pathological examinations were limited to one rat per dose level. The decabromodiphenyl oxide used in this study was 77.4% pure.

Respiratory difficulty, eye squint and ocular discharge were noted in the male and female rats that were exposed by inhalation to 2 or 48.2 mg/ℓ decabromodiphenyl oxide (97% pure) for 1 hour (Great Lakes, 1984). Incidences of these effects were not reported in the secondary review of this study, but 20 rats/dose level were tested and all rats were normal within 14 days.

Application of dry decabromodiphenyl ether (77.4% pure) to intact Sprague-Dawley rabbit skin for 24 hours caused no response, but application to occluded abraded skin for 24 hours, abraded skin for 3 days or intact skin for 5 hours/day for 2 weeks, resulted in a slight erythematous and edematous response (Norris et al., 1973, 1975). The responses subsided with cessation of treatment; effects on appearance, demeanor or body weights were not observed. Application of dry decabromodiphenyl ether to the washed or unwashed eyes of rabbits caused transient conjunctival irritation (Norris et al., 1973, 1975).

Skin sensitization was not induced in 50 human subjects by topical application of a 5% suspension of decabromodiphenyl oxide (77.4% pure) in petrolatum (method and quantity of application not reported) 3 times/week for 3 weeks or on challenge 2 weeks following the final treatment (Norris et al., 1973, 1975).

5.7. SUMMARY

Decabromodiphenyl oxide was tested for carcinogenicity in an NTP (1985) bioassay in which diets containing 0, 25,000 or 50,000 ppm of commercial grade compound (94-97% pure) were administered to groups of 50 male and 50 female F344-N rats and 50 male and 50 female B6C3F1 mice for 103 weeks. Daily dosages, estimated from food consumption data, were in the range of 1100-1200 and 2250-2500 mg/kg/day for the low- and high-dose rats and 3200-3800 and 6650-7800 mg/kg/day for the low- and high-dose mice. Some evidence of carcinogenicity was indicated by significantly increased incidences of liver neoplastic nodules in the rats (low- and high-dose males, high-dose females). Equivocal evidence of carcinogenicity, as indicated by significantly increased incidences of hepatocellular adenomas or carcinomas (combined) and the presence of thyroid gland tumors (adenomas or carcinomas), was found for male mice. Evidence of carcinogenicity was not observed in another dietary study in which groups of 25 male and 25 female Sprague-Dawley rats were adminis- tered much lower doses (0, 0.01, 0.1 or 1.0 mg/kg/day) of less pure (77.4%) compound for 2 years (Kociba et al., 1975; Norris et al., 1973, 1975).

Mutagenicity of decabromodiphenyl oxide was not demonstrated with or without metabolic activation in liquid suspension Ames assays with Salmonella typhimurium TA1535, TA1537, TA98 or TA100, in a mouse lymphoma L5178Y/TK$^{+/-}$ assay or in sister chromatid exchange or chromosomal aberrations assays in Chinese hamster ovary cells (NTP, 1985). Dietary administration of decabromodiphenyl oxide (77.4% pure) at doses of 0, 3, 30 or 100 mg/kg bw/day for 90 days before and during mating, gestation and lactation did not produce treatment-related increases in cytogenetic aberrations in bone marrow cells in maternal or neonatal Sprague-Dawley rats examined at weaning (Norris et al., 1975).

Teratogenicity or maternal toxicity was not observed in Sprague-Dawley rats administered 0, 10, 100 or 1000 mg/kg decabromodiphenyl oxide (77.4% pure) in corn oil by gavage on days 6-15 of gestation (Norris et al., 1973, 1975). Fetotoxicity was indicated by increased incidences of subcutaneous edema and delayed ossification of normally developed skull bones at 1000 mg/kg and resorptions at 10 and 100 mg/kg. Effects on reproductive capacity and neonatal development were not observed in Sprague-Dawley rats and offspring that were maintained on diets that provided 0, 3, 30 or 100 mg/kg/day decabromodiphenyl oxide (77.4% pure) for 90 days before and during mating, gestation and lactation (Norris et al., 1975).

Treatment-related nonneoplastic lesions were observed in the NTP (1985) carcinogenesis bioassay in which F344-N rats and B6C3F1 mice of each sex were administered diets containing 0, 25,000 or 50,000 ppm decabromodiphenyl oxide (94-97%) for 103 weeks. Lesions included thrombosis and degeneration of the liver, fibrosis of the spleen, lymphoid hyperplasia of the mandibular lymph nodes and acanthosis of the forestomach in the high-dose male rats and hematopoiesis in the spleen in treated female rats. Nonneoplastic lesions in male mice included hypertrophy in the liver (low and high dose), granulomas in the liver (low dose) and follicular cell hyperplasia of the thyroid (low and high dose). An increased incidence of ulcers of the stomach occurred in the high-dose female mice. Dietary administration of 0, 3100, 6200, 12,500, 25,000 or 50,000 ppm decabromodiphenyl oxide for 13 weeks did not produce treatment-related effects (NTP, 1985).

No effects were observed in Sprague-Dawley rats that were administered diets providing decabromodiphenyl oxide (77.4% pure) dosages of 0, 0.01, 0.1 or 1.0 mg/kg/day for ~2 years (Kociba et al., 1975; Norris et al., 1973, 1975). Male Sprague-Dawley rats fed diets providing approximate doses of 0,

8, 80 or 800 mg/kg/day for 30 days had increased liver weights at 80 and 800 mg/kg/day, histological alterations in the liver (centrilobular cytoplasmic enlargement and vacuolation) and kidneys (hyaline degenerative cytoplasmic changes) at 800 mg/kg/day, and thyroid hyperplasia at 80 and 800 mg/kg/day (Norris et al., 1973, 1975).

6. AQUATIC TOXICITY

6.1. ACUTE

Pertinent data regarding acute toxicity of decabromodiphenyl oxide to aquatic organisms could not be located in the available literature as cited in the Appendix.

6.2. CHRONIC

Pertinent data regarding chronic toxicity of decabromodiphenyl oxide to aquatic organisms could not be located in the available literature as cited in the Appendix.

6.3. PLANTS

Pertinent data regarding chronic toxicity of decabromodiphenyl oxide to aquatic organisms could not be located in the available literature as cited in the Appendix.

6.4. RESIDUES

Norris et al. (1973) conducted a study in which rainbow trout, Salmo gairdneri, were exposed to 20 µg/ℓ ^{14}C-decabromodiphenyl oxide for 48 hours. The compound did not accumulate in fish muscle (fillets) to a measurable extent. The concentration of ^{14}C-decabromodiphenyl oxide in water remained constant during the experiment, indicating that no uptake occurred.

6.5. SUMMARY

Norris et al. (1973) found that rainbow trout did not accumulate decabromodiphenyl oxide to a measurable extent when exposed to 20 µg/ℓ for 48 hours.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Occupational exposure limits for decabromodiphenyl oxide are not recommended by NIOSH or ACGIH or proposed by OSHA. The American Industrial Hygiene Association recommends a Workplace Environmental Exposure Level (WEEL) of 5 mg/m³ as an 8-hour TWA for a 40-hour workweek (AIHA, 1981).

An ADI of 0.7 mg/day was derived for decabromodiphenyl oxide by the U.S. EPA (1983) from a NOAEL of 1.0 mg/kg/day established in a 2-year oral (diet) study with rats (Kociba et al., 1975; Norris et al., 1973, 1975) using an uncertainty factor of 100. The ADI was calculated before availability of an NTP (1985) bioassay indicating carcinogenicity of decabromodiphenyl oxide.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic biota from the effects of decabromodiphenyl oxide could not be located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

Decabromodiphenyl oxide was tested for carcinogenicity in an NTP (1985) bioassay in which diets containing 0, 25,000 or 50,000 ppm of commercial grade compound (94-97% pure) were administered to groups of 50 F344-N rats and 50 B6C3F1 mice of each sex for 103 weeks. Daily dosages, estimated from food consumption data, were in the range of 1100-1200 and 2250-2500 mg/kg/day for the low- and high-dose rats and 3200-3800 and 6650-7800 mg/kg/day for the low- and high-dose mice. Some evidence for carcinogenicity was indicated by significantly increased incidences of liver neoplastic nodules in the rats (low- and high-dose males, high-dose females). Equivocal evidence of carcinogenicity as indicated by significantly increased incidences of hepatocellular adenomas or carcinomas (combined) and the presence of thyroid tumors in the treated male mice was found. Evidence of carcinogenicity was not observed in another diet study in which groups of 25 male and 25 female Sprague-Dawley rats were administered much lower doses (0, 0.01, 0.1 or 1.0 mg/kg/day) of a less pure (77.4%) compound for 2 years (Kociba et al., 1975; Norris et al., 1973, 1975).

Mutagenicity of decabromodiphenyl oxide was not demonstrated with or without metabolic activation in liquid suspension Ames assays with Salmonella typhimurium TA1535, TA1537, TA98 or TA100, in a mouse lymphoma L5178Y/TK$^{+/-}$ assay or in sister chromatid exchange or chromosomal aberration assays in Chinese hamster ovary cells (NTP, 1985). Dietary administration of decabromodiphenyl oxide (77.4% pure) at doses of 0, 3, 30 or 100 mg/kg bw/day for 90 days before and during mating, gestation and lactation did not produce treatment-related increases in cytogenetic aberrations in bone marrow cells in maternal or neonatal Sprague-Dawley rats examined at weaning (Norris et al., 1975).

Teratogenicity or maternal toxicity was not observed in Sprague-Dawley rats administered 0, 10, 100 or 1000 mg/kg decabromodiphenyl oxide (77.4% pure) in corn oil by gavage on days 6-15 of gestation (Norris et al., 1973, 1975). Fetotoxicity was indicated by increased incidences of subcutaneous edema and delayed ossification of normally developed skull bones at 1000 mg/kg and resorptions at 10 and 100 mg/kg. Effects on reproductive capacity and neonatal development were not observed in Sprague-Dawley rats and offspring that were maintained on diets that provided 0, 3, 30 or 100 mg/kg/day decabromodiphenyl oxide (77.4% pure) for 90 days before and during mating, gestation and lactation (Norris et al., 1975).

Treatment-related nonneoplastic lesions were observed in the NTP (1985) carcinogenesis bioassay in which F344-N rats and B6C3F1 mice of each sex were administered diets containing 0, 25,000 or 50,000 ppm decabromodiphenyl oxide (94-97%) for 103 weeks as detailed previously. These included thrombosis and degeneration of the liver, fibrosis of the spleen, lymphoid hyperplasia of the mandibular lymph nodes and acthosis of the forestomach in the high-dose male rats and hematopoiesis in the spleen in treated female rats. Nonneoplastic lesions in the male mice included hypertrophy in the liver (low and high dose), granulomas in the liver (low dose) and follicular cell hyperplasia of the thyroid (low and high dose). An increased incidence of ulcers of the stomach occurred in the high-dose female mice. Treatment-related effects on clinical signs, body weight, food consumption or survival were not observed in any of the groups of rats or mice. Dietary administration of 0, 3100, 6200, 12,500, 25,000 or 50,000 ppm decabromodiphenyl oxide for 13 weeks did not produce treatment-related effects on the aforementioned parameters, including tissue histology, in groups of 10 F344-N rats and 10 B6C3F1 mice of each sex in NTP (1985) carcinogenesis bioassay range-finding studies.

Toxicity as evaluated by clinical observations, body weight and food measurements, urine and blood (hematology and clinical chemistry) analyses, and gross and histological examinations was not observed in groups of 25 Sprague-Dawley rats of each sex that were administered diets that provided decabromodiphenyl oxide dosages of 0, 0.01, 0.1 or 1.0 mg/kg/day for ~2 years (Kociba et al., 1975; Norris et al., 1973, 1975). In addition to providing much lower dosages than the NTP (1985) bioassay, this study used a compound of lower purity (77.4%). Groups of five male Sprague-Dawley rats were also fed diets containing 0, 0.01, 0.1 or 1.0% decabromodiphenyl oxide of the same composition (reportedly providing approximate doses of 0, 8, 80 or 800 mg/kg/day, respectively) for 30 days and similarly evaluated (Norris et al., 1973, 1975). Effects were only indicated by necropsy and included (incidences not reported) increased liver weights at 80 and 800 mg/kg/day, histological alterations in the liver (centrilobular cytoplasmic enlargement and vacuolation) and kidneys (hyaline degenerative cytoplasmic changes) at 800 mg/kg/day, and thyroid hyperplasia at 80 and 800 mg/kg/day.

Based on the histopathological findings of neoplastic nodules in the livers of low- and high-dose male rats and high-dose female rats, NTP (1985) concluded that there was some evidence of carcinogenicity of decabromodiphenyl oxide. Increased incidences of hepatocellular adenomas or carcinomas (combined) occurred at statistically significant levels ($p<0.02$ for Fischer Exact tests, $p=0.027$ for Cochran-Armitage trend test) in the dosed male mice (NTP, 1985), but interpretation of these data is complicated by early nontreatment-related mortality of the control animals and lack of a dose-related response. These considerations and the less than significant ($p>0.05$) increased incidences of thyroid gland follicular cell adenomas or carcinomas were interpreted as providing equivocal evidence of carcinogenicity for the male mice.

A risk assessment for decabromodiphenyl oxide previously performed by the U.S. EPA (1983) derived an ADI from the 2-year diet study reported by Norris et al. (1973, 1975) and Kociba et al. (1975). The NTP (1985) bioassay data were not available for that assessment.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) BASED ON CHRONIC TOXICITY

Diets containing 0, 25,000 or 50,000 ppm of commercial grade decabromodiphenyl oxide (94-97% pure) were administered to groups of 50 F344/N rats and 50 B6C3F1 mice of each sex for 103 weeks in an NTP (1985) carcinogenesis bioassay. Daily dosages, estimated from food consumption data, were 1119 and 2236 mg/kg for the low- and high-dose male rats, 1199 and 2553 mg/kg for the low- and high-dose female rats, 3203 and 6645 mg/kg for the low- and high-dose male mice, and 3758 and 7776 mg/kg in the low- and high-dose female mice. Treatment-related nonneoplastic lesions observed at necropsy (104 weeks in the rats, 103-104 weeks in the mice) included thrombosis and degeneration of the liver, fibrosis of the spleen, lymphoid hyperplasia of the mandibular lymph nodes and acanthosis of the forestomach in the high-dose male rats and hematopoiesis in the spleen in treated female rats. Non-neoplastic lesions in the male mice included hypertrophy in the liver (low and high dose), granulomas in the liver (low dose) and follicular cell hyperplasia of the thyroid (low and high dose). An increased incidence of ulcers of the stomach occurred in the high-dose female mice. Treatment-related effects on clinical signs, body weight, food consumption or survival were not observed in any of the groups of rats or mice. Dietary administration of 0, 3100, 6200, 12,500, 25,000 or 50,000 ppm decabromodiphenyl oxide for 13 weeks did not produce treatment-related effects on the aforementioned parameters, including tissue histology, in groups of 10 F344/N rats and 10 B6C3F1 mice of each sex in NTP (1985) carcinogenesis bioassay range-finding studies. In addition, d[illegible]y concentrations up to 100,000 ppm for 14 days were without effect in rats and m[illegible] (NTP, 1985).

Toxicity as evaluated by clinical observations, body weight and food measurements, urine and blood (hematology and clinical chemistry) analyses, and gross and histological examinations was not observed in groups of 25 male and 25 female Sprague-Dawley rats that were administered diets providing decabromodiphenyl oxide dosages of 0, 0.01, 0.1 or 1.0 mg/kg/day for ~2 years (Kociba et al., 1975; Norris et al., 1973, 1975). In addition to providing much lower dosages than the NTP (1985) bioassay, these studies used a compound of lower purity (77.4% decabromodiphenyl oxide, 21.8% nonabromodiphenyl oxide, 0.8% octabromodiphenyl oxide). Groups of five male Sprague-Dawley rats were also fed diets containing 0, 0.01, 0.1 or 1.0% decabromodiphenyl oxide of the same composition (reportedly providing approximate doses of 0, 8, 80 or 800 mg/kg/day, respectively) for 30 days and similarly evaluated (Norris et al., 1973, 1975). Effects were only indicated by necropsy and included (incidences not reported) increased liver weights at 80 and 800 mg/kg/day, histological alterations in the liver (centrilobular cytoplasmic enlargement and vacuolation) and kidneys (hyaline degenerative cytoplasmic changes) at 800 mg/kg/day, and thyroid hyperplasia at 80 and 800 mg/kg/day.

Teratogenicity or maternal toxicity was not observed in a study in which unspecified numbers of Sprague-Dawley rats were administered 0, 10, 100 or 1000 mg/kg decabromodiphenyl oxide (77.4% pure) in corn oil by gavage on days 6-15 of gestation (Norris et al., 1973, 1975). Fetotoxicity was indicated by increased incidences of subcutaneous edema and delayed ossification of normally developed skull bones at 1000 mg/kg and resorptions at 10 and 100 mg/kg, but the incidences and the number of fetuses examined were not specified. Effects on reproductive capacity and neonatal development were not observed in an unspecified number of Sprague-Dawley rats and offspring that were maintained on diets that provided 0, 3, 30 or 100 mg/kg/day

decabromodiphenyl oxide (77.4% pure) for 90 days before and during mating, gestation and lactation (Norris et al., 1975).

The only experiments in which effects were observed, therefore, were the 2-year studies in F344 rats and B6C3F1 mice in the NTP (1985) carcinogenesis bioassay and the teratogenicity study and 30-day study in Sprague-Dawley rats (Norris et al., 1973, 1975). These studies are summarized in Table 9-1. The effects on the liver, kidney and spleen observed at 80 or 800 mg/kg/day in the 30-day study by Norris et al. (1973, 1975) cannot be considered for RQ determination because, although these effects occurred at doses much lower than those used in the 2-year bioassay by NTP (1985), the compound was considerably less pure. Moreover, NTP (1985) found no effects in rats and mice administered 94-97% pure decabromodiphenyl oxide in the diet at up to 50,000 ppm for 13 weeks and up to 100,000 ppm for 14 days.

The fetotoxic effects in the teratogenicity study by Norris et al. (1973, 1975) likewise were observed with the less pure compound, and the study was reported in too limited detail to assess the significance of the results. Therefore, this study will not be considered for RQ determination.

The data used to calculate CSs and RQs are presented in Table 9-2. The animal transformed doses were converted to human MEDs by multiplying by the cube root of the ratio of the animal weight to the reference human weight (70 kg) and by 70 kg to express in units of mg/day. The animal weights used in these calculations were reported by NTP (1985) as indicated in Table 9-1. All of the human MEDs correspond to an RV_d of 1. Increased hematopoiesis of the spleen warrants an RV_e of 2. The effects of fibrosis in the spleen and lymphoid hyperplasia in the male F344/N rats (NTP, 1985) are considered consistent with an RV_e of 6 because of the presumed irreversibility of

TABLE 9-1

Oral Toxicity Summary for Decabromodiphenyl Oxide

Species/ Strain	Sex	No. at Start	Average Weight (kg)	Vehicle/ Physical State	Purity	Exposure	Transformed Animal Dose (mg/kg/day)	Response	Reference
Rat/F344/N	F	50	0.25[a]	diet	94-97%	25,000 ppm 103 weeks	1199[b]	Hematopoiesis of the spleen	NTP, 1985
Rat/F344/N	F	50	0.25[a]	diet	94-97%	50,000 ppm 103 weeks	2553[b]	Hematopoiesis of the spleen	NTP, 1985
Rat/F344/N	M	50	0.40[a]	diet	94-97%	50,000 ppm 103 weeks	2236[b]	Thrombosis and degeneration of the liver, fibrosis of the spleen, lymphoid hyperplasia, acanthosis of the forestomach	NTP, 1985
Mouse/ B6C3F1	M	50	0.04[a]	diet	94-97%	25,000 ppm 103 weeks	3203[b]	Centrilobular hypertrophy and granulomas of the liver; follicular cell hyperplasia of thyroid	NTP, 1985
	M	50	0.04[a]	diet	94-97%	50,000 ppm 103 weeks	6645[b]	Centrilobular hypertrophy of the liver (no granulomas); follicular cell hyperplasia of thyroid	NTP, 1985
	F	50	0.04[a]	diet	94-97%	50,000 ppm 103 weeks	7776[b]	Ulcers of the stomach	NTP, 1985
Rat/Sprague-Dawley	M	5	0.35[c]	diet	77.4%	0.1% for 30 days	80[b]	Increased liver weight, thyroid hyperplasia	Norris et al., 1973, 1975
	M	5	0.35[c]	diet	77.4%	1.0% for 30 days	800[b]	Increased liver weight, centrilobular cytoplasmic enlargement and vacuolation in liver, hyaline degenerative cytoplasmic changes in kidney, thyroid hyperplasia	Norris et al., 1973, 1975
Rat/Sprague-Dawley	F	NR	0.35[c]	gavage/ corn oil	77.4%	1000 mg/kg/ day on days 6-15 of gestation	1000	Fetotoxicity (subcutaneous edema and delayed ossification of skull bones)	Norris et al., 1973, 1975

[a]Estimated from growth curves in report

[b]Estimated average daily dose from report

[c]Reference body weight of rats from U.S. EPA (1980)

NR = Not reported

TABLE 9-2

Composite Scores for Oral Toxicity of Decabromodiphenyl Oxide*

Species/ Strain	Sex	Animal Dose (mg/kg/day)	Chronic Human MED (mg/day)	RV_d	Effect	RV_e	CS	RQ
Rat/ F344/N	F	1119 (103 weeks)	11,973	1	Increased hematopoiesis of spleen	2	2	5000
Rat/ F344/N	M	2236 (103 weeks)	27,982	1	Thrombosis and degeneration of liver, fibrosis of spleen, lymphoid hyperplasia, acanthosis of forestomach	6	6	1000
Mouse/ B6C3F1	M	3203 (103 weeks)	18,606	1	Centrilobular hypertrophy of liver, follicular cell hyperplasia of thyroid	3	3	5000
Mouse/ B6C3F1	F	7776 (103 weeks)	45,169	1	Ulcers of stomach	6	6	1000

*Source: NTP, 1985

these lesions; the liver thrombosis and unspecified degeneration is not inconsistent with this RV_e, but there were neoplastic alterations in the same organs. The centrilobular hypertrophy of the liver and follicular cell hyperplasia of the thyroid in the male B6C3F1 mice (NTP, 1985) is assigned an RV_e of 3. The stomach ulcers in the female B6C3F1 mice (NTP, 1985) are consistent with a RV_e of 6 because it represents a necrotic alteration with no apparent decrement in function (treatment-related effects on body weight or food consumption were not observed). The highest CSs (product of RV_d and RV_e) of 6, corresponding to RQs of 1000, were obtained for the effects in the liver, spleen and forestomach of male rats and for the stomach ulcers in female mice. Since the effects in rats occurred at a lower MED, these data are recommended as the basis of the RQ (Table 9-3).

In a previous determination, U.S. EPA (1983) based the RQ of 1000 on the fetotoxicity observed in the teratogenicity study of Norris et al. (1973, 1975); however, the NTP (1985) subchronic and chronic studies using much purer compound were not available to U.S. EPA (1983). Teratogenicity and fetotoxicity of the purer compound have not been investigated; nevertheless, the RQ derived in the present determination is also 1000.

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Decabromodiphenyl oxide was tested for carcinogenicity in an NTP (1985) bioassay in which diets containing 0, 25,000 or 50,000 ppm of commercial grade compound (94-97% pure) were administered to groups of 50 F344/N rats and 50 B6C3F1 mice of each sex for 103 weeks. Daily dosages, estimated from food consumption data, were in the range of 1100-1200 and 2250-2500 mg/kg/day for the low- and high-dose rats and 3200-3800 and 6650-7800 mg/kg/day for the low- and high-dose mice. As detailed in Table 5-1, evidence for carcinogenicity is indicated by significantly increased incidences of liver

TABLE 9-3

Decabromodiphenyl Oxide

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	oral
Dose*:	27,982 mg/day
Effect:	thrombosis and degeneration of liver, fibrosis of spleen, lymphoid hyperplasia, acanthosis of forestomach
Reference:	NTP, 1985
RV_d:	1
RV_e:	6
Composite Score:	6
RQ:	1000

*Equivalent human dose

neoplastic nodules in the rats (low- and high-dose males, high-dose females). Incidences of hepatocellular adenomas or carcinomas (combined) were significantly increased in the treated male mice. Follicular cell adenomas or carcinomas (combined) of the thyroid occurred in the treated male mice, but the increases were not statistically significant. Evidence of carcinogenicity was not observed in another diet study in which groups of 25 male and 25 female Sprague-Dawley rats were administered much lower doses (0, 0.01, 0.1 or 1.0 mg/kg/day) of less pure compound (77.4% decabromodiphenyl oxide, 21.8% nonabromodiphenyl oxide and 0.8% octabromodiphenyl oxide) for 2 years (Kociba et al., 1975; Norris et al., 1973, 1975).

Mutagenicity of decabromodiphenyl oxide was not demonstrated in liquid suspension. Ames assays with Salmonella typhimurium TA1535, TA1537, TA98 or TA100 or in a mouse lymphoma L5178Y/TK$^{+/-}$ assay (NTP, 1985). Sister chromatid exchange or chromosomal aberrations were not induced in Chinese hamster ovary cells treated with decabromodiphenyl oxide in vitro (NTP, 1985). The above NTP (1985) assays were conducted with and without mammalian liver S-9 metabolic activation preparations and apparently used the commercial grade decabromodiphenyl oxide used in the NTP (1985) carcinogenesis bioassay. Dietary administration of decabromodiphenyl oxide (77.4% pure) at doses of 0, 3, 30 or 100 mg/kg bw/day for 90 days before and during mating, gestation and lactation did not produce treatment-related increases in cytogenetic aberrations in bone marrow cells in maternal or neonatal Sprague-Dawley rats examined at weaning (Norris et al., 1975).

Based on the histopathological findings of neoplastic nodules in the liver of the low- and high-dose male rats and high-dose female rats, NTP (1985) concluded that there was some evidence of carcinogenicity of decabromodiphenyl oxide. Increased incidences of hepatocellular adenomas or

carcinomas (combined) occurred at statistically significant levels ($p<0.02$ for Fischer Exact tests, $p=0.027$ for Cochran-Armitage trend test) in the dosed male mice (NTP, 1985), but interpretation of these data is complicated by early nontreatment-related mortality of control animals. This consideration and the less than significant ($p>0.05$) increased incidences of thyroid gland follicular cell adenomas or carcinomas were interpreted by NTP as providing equivocal evidence of carcinogenicity for the male mice. The overall weight of evidence for carcinogenicity from the animal studies is consistent with IARC Group 3 and CAG Group C (Possible Human Carcinogen) (U.S. EPA, 1986).

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Sasaki, S. 1978. The scientific aspects of the chemical substance control law in Japan. In: Aquatic Pollutants: Transformation and Biological Effects, O. Hutzinger, L.H. Von Letyoeld and B.C.J. Zoeteman, Ed. Pergamon Press, Oxford. p. 283-298.

SRI (Stanford Research Institute). 1985. 1985 Directory of Chemical Producers: United States of America. SRI International, Menlo Park, CA. p. 511.

Tabak, H.H., S.A. Quave, C.I. Mashni and E.F. Barth. 1981. Biodegradability studies with organic priority pollutant compounds. J. Water Pollut. Control Fed. 53: 1503-1518.

U.S. EPA. 1980. Guidelines and Methodology Used in the Preparation of Health Effects Assessment Chapters of the Consent Decree Water Criteria Documents. Federal Register. 45(231): 49347-49357.

U.S. EPA. 1983. Health and Environmental Effects Profile for Brominated Diphenyl Ethers. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1985. Reportable Quantity Document for Brominated Diphenyl Ethers. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC.

U.S. EPA. 1986. Guidelines for Carcinogen Risk Assessment. Federal Register. 51(185): 33992-34003.

USITC (U.S. International Trade Commission). 1983. Imports of Benzenoid Chemicals and Products 1982. USITC Publ. 1401, Washington, DC. p. 14.

Yagi, O. and R. Sudo. 1980. Degradation of polychlorinated biphenyls by microorganisms. J. Water Pollut. Control Fed. 52(5): 1035-1043.

APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

GLOBAL
TSCATS
CASR online (U.S. EPA Chemical Activities Status Report)
CAS online STN International
TOXLINE
TOXBACK 76
TOXBACK 65
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP
NTIS
Federal Register

These searches were conducted in April, 1986. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the Threshold Limit Values and Biological Exposure Indices, 5th ed. Cincinnati, OH.

ACGIH (American Conference of Governmental Industrial Hygienists). 1985-1986. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1985-1986. Cincinnati, OH. 114 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. 2878 p.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1983. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology, 3rd ed. Publishing Sciences Group, Inc., Littleton, MA. 575 p.

IARC (International Agency for Research on Cancer). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans. WHO, IARC, Lyons, France.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. 700 p.

NTP (National Toxicology Program). 1986. Toxicology Research and Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, N.I. 1979. Dangerous Properties of Industrial Materials, 5th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1984. Directory of Chemical Producers. Menlo Park, CA.

U.S. EPA. 1985. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call in Programs. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1985. CSB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (U.S. International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982, USITC Publ. 1422, Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

Windholz, M., Ed. 1983. The Merck Index, 10th ed. Merck and Co., Inc., Rahway, NJ.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under Contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. U.S. Dept. Interior, Fish and Wildlife Serv. Res. Publ. 137, Washington, DC.

McKee, J.E. and H.W. Wolf. 1963. Water Quality Criteria, 2nd ed. Prepared for the Resources Agency of California, State Water Quality Control Board. Publ. No. 3-A.

Pimental, D. 1971. Ecological Effects of Pesticides on Non-Target Species. Prepared for the U.S. EPA, Washington, DC. PB-269605.

Schneider, B.A. 1979. Toxicology Handbook. Mammalian and Aquatic Data. Book 1: Toxicology Data. Office of Pesticide Programs, U.S. EPA, Washington, DC. EPA 540/9-79-003. NTIS PB 80-196876.